Applicants respectfully disagree with the Examiner's assertion that the specification is allegedly not enabling for a method of protecting neuronal cells from death in a subject having or at risk of having a neuropathological disorder. In an attempt to support this assertion, the Examiner states that the specification does not include working examples to indicate that administration of protein C (APC) to a subject protects neuronal cells from death. Contrary to the Examiner's assertion, it is respectfully submitted that working examples are indeed provided as the data set forth in the Examples explicitly illustrate that administration of activated protein C (APC) protects neuronal cells from cell death. In particular, the data in Examples 1 and 2 demonstrate that treatment with protein C (APC) either before or after induction of stroke protected mice from accelerated stroke-related death and restored cerebral blood flow during middle cerebral artery occlusion (see specification, pages 30-31). Clearly, administration of protein C (APC) results in significant reduction in brain injury with a concomitant improvement in neurological performance. Therefore, those skilled in the art would readily acknowledge that the specification enables methods for protecting neuronal cells from cell death.

Furthermore, Applicants respectfully disagree with the Examiner's assertion that the present specification is allegedly not enabling for a method of reducing inflammation in a subject having or at risk of having a neuropathological disorder. In an attempt to support this assertion, the Examiner states that the specification does not include working examples to indicate that administration of protein C (APC) to a subject reduces inflammation. Contrary to the Examiner's assertion, the present specification provides data which demonstrates that administration of protein C (APC) reduced volumes of brain infarction and edema by 59% and 50%, respectively (see, e.g., page 10, lines 3-4; page 31, lines 18-24; page 33, lines 22-26).

Moreover, Applicants disagree with the Examiner's assertion that undue experimentation would allegedly be required to determine the optimal quantity of protein C (APC) administration, the best route of administration, the duration of treatment, and possible side effects produced by administration of protein C (APC). Those skilled in the art would readily acknowledge that these factors are all simply administration protocols which vary depending on the disease being treated and the size and general health of the subject undergoing treatment. Accordingly, any alleged "experimentation" required to optimize these factors would only be routine experimentation, and therefore would not rise to the level of undue experimentation.

Applicants respectfully submit that the guidance provided by the specification (including the working examples), combined with the general knowledge of those skilled in the art, fully enables the entire scope of the present claims. Accordingly, reconsideration and withdrawal of the rejection of claims 1-16 and 19-21 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

C. Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 1-16 and 19-21 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, is respectfully traversed. With specific reference to the phrases "neuroprotective amount" and "anti-inflammatory effective amount", Applicants respectfully disagree with the Examiner's assertion that these phrases render claims 1-16 and 19-21 indefinite. When these phrases are construed in light of the specification, it is clear that "neuroprotective amount" and "anti-inflammatory effective amount" refer to dosages which necessarily vary depending on the disease being treated and on the size and general health of the subject undergoing treatment. Those skilled in the art are readily able to determine appropriate dosage ranges by routine manipulation of standard administration protocols, which are set forth in detail in the specification (see page 19, line 14 to page 22, line 16). In particular, specific dosage ranges are set forth in the specification

(see page 21, line 19, to page 22, line 10). Thus, the Examiner's assertion that appropriate dosage ranges allegedly can not be determined is respectfully submitted to be in error. Accordingly, reconsideration and withdrawal of the rejection of claims 1-16 and 19-21 under 35 U.S.C. § 112, second paragraph are respectfully requested.

D. Rejection Under 35 U.S.C. § 102(b)

The rejection of claims 1, 2, 9, 10, and 15 under 35 U.S.C. 102(b) as allegedly being anticipated by Griffin, et. al. (U.S. Patent No. 5,084,274), is respectfully traversed. Applicants' invention, as defined for example, by claim 1, distinguishes over Griffin by requiring a method of protecting neuronal cells from cell death in a subject having or at risk of having a neuropathological disorder, comprising administering to the subject a neuroprotective amount of activated protein C (APC), thereby providing neuroprotection to the subject. Griffin does not describe such a method. Instead, Griffin describes a method for preventing arterial thrombotic occlusion. Indeed, Griffin is silent with respect to methods for protecting neuronal cells from cell death in a subject having or at risk of having a neuropathological disorder.

To support this anticipation rejection, the Examiner's asserts that the preamble of a claim is generally not accorded patentable weight and therefore Griffin allegedly anticipates the subject matter recited in the body of the claim. However, whether a preamble should be accorded patentable weight is a fact specific analysis that is "...determined on the facts of each case in light of the overall form of the claim, and the invention as described in the specification..." (*Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc.*, 98 F.3d 1563, 1572-73, 40 USPQ2d 1481, 1488 (Fed. Cir. 1996), emphasis added).

When the overall language of claim 1 is considered, and, when claim 1 is construed in light of the specification, it is clear that the invention is drawn to "a method of protecting neuronal cells from cell death in a subject having or at risk of having a neuropathological disorder" (as stated in the preamble). The body of present claim 1 recites "...administering to the subject a neuroprotective amount of activated protein C (APC), thereby providing

neuroprotection to the subject." The preamble and the body of claim 1 are thereby linked based upon the neuroprotective benefit realized by activated protein C (APC) administration. Indeed, since the neuroprotecive benefits of activated protein C (APC) administration are discussed throughout the specification, and recited in both the preamble and the body of claim 1, it is clear that the preamble of present claim 1 is to be considered when making an anticipation determination. Moreover, the accompanying Declaration and the Exhibits attached thereto provide further confirmatory evidence that activated protein C (APC) is directly neuroprotective.

When claim 1 is properly construed, including consideration of the preamble, it is clear that the invention is not, as characterized by the Examiner, merely administration of activated protein C (APC). Instead, the present invention distinguishes over Griffin by requiring a method of protecting neuronal cells from cell death in a subject having or at risk of having a neuropathological disorder (preamble), comprising administering to the subject a neuroprotective amount of activated protein C (APC), thereby providing neuroprotection to the subject (body). Since Griffin is silent with respect to neuroprotection of any kind, Griffin can not anticipate the present invention. Accordingly, reconsideration and withdrawal of the rejection of claims 1, 2, 9, 10, and 15 under 35 U.S.C. 102(b) are respectfully requested.

CONCLUSION

In view of the above amendment and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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